Serial No.: 10/798,592
Group Art Unit 1615
Examiner Isis A. D. Ghali

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STATUS OF CLAIMS

Claims 1-39 are pending in the application. Claims 23-39 are withdrawn from consideration pursuant to a restriction requirement. Thus, claims 1-22 are currently under examination. Claims 1, 5 and 9 have been amended. Support for the amendment to claim 1 is provided in the original claims as filed. Support for the amendment to claim 5 is provided, *inter alia*, in paragraph [0017] of the specification. Support for the amendment to claim 9 is provided, *inter alia*, in original claim 1 and paragraphs [0017] to [0019] of the specification. There is no issue of new matter.

REMARKS

Rejection Under 35 U.S.C. 112, second paragraph

Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states that Claim 1 recites single first nitric oxide donor (NO) compound and single second nitric oxide donor compound in the 2nd and 3rd lines of the claims. However, the Examiner points out that the claim recites that "one or more of said nitric oxide donor compound" in the 6th and 8th lines of the claim and thus, it is unclear how one or more compounds will be delivered if one compound is recited. In addition, regarding Claim 1, the Examiner states that there is insufficient antecedent basis for the term "product." Regarding Claim 5, the Examiner states that it recites that the first NO compound has a short half-life and the second NO donor has a long half-life while Claim 8 recites the opposite. Regarding Claim 9, the Examiner states that there is insufficient antecedent basis for the term "vasculature."

In response, Applicants have amended Claims 1, 5, and 9 to obviate the rejections. Regarding the Examiner's objection to the term "product" in Claim 1, however, Applicants point out that they are the first occurrences of the term and they do not require a further antecedent basis. Specifically, the claim provides for "a nitric oxide product of said first nitric oxide donor compound" and "a nitric oxide product of said second nitric oxide donor compound." Both such products are prefaced with the indefinite article, "a," and indicate

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products of the first and second nitric oxide donor compounds. As taught in the specification, a nitric oxide donor compound can "release[] nitric oxide" and other nitric oxide donor compounds release nitric oxide after being converted to another compound (see paragraphs [0015] and [0020]). Applicants thus state that the word "product" is not indefinite and complies with the requirements of 35 U.S.C. 112, second paragraph and respectfully requests that the Examiner reconsider and withdraw the objection.

Rejection for Non-Statutory Double Patenting

Claims 1-22 are rejected under the non-statutory doctrine of double patenting of the obviousness type over claims 1-23 of U.S. Pat. No. 6,706,274.

In response, Applicant hereby submits a terminal disclaimer to obviate the rejection.

Rejection under 35 USC § 103(a) over Michal et al.

Claims 1-22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. No. 6,287,285 (Michal et al.) in combination with the article, "S-Nitrosothiols cause prolonged, nitric oxide mediated relaxation in human saphenous vein and internal mammary artery: therapeutic potential in bypass surgery" by Sogo et al.

In response, Applicants respectfully traverse the rejections and their accompanying remarks. Applicants state that the Examiner has not met his burden of establishing a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claimed features. In addition, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

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Applicants state that the rejection fails at least because of the fundamental defects of Michal et al. which are not remedied by the secondary reference, Sogo et al. The prior art references, in combination, fail to teach or suggest all the claim limitations. Specifically, Michal et al. fails to teach a ***combination of two NO donor compounds*** in the medical device. Indeed, the Examiner herself agrees that "the reference ***suggested*** inclusion of more than one NO donor in the medical device...however, the reference ***does not explicitly teach*** the combination of S-nitroso-N-acetyl-D,L-pencillamine and S-nitrosoglutathione" (emphasis added). Michal et al. fails to provide any explicit statement of using a combination of NO donor compounds. Indeed, Applicants assert that Michal et al. does not even "suggest" inclusion of more than one NO donor compounds, and the only passage of Michal et al. that the Examiner turns to support her argument that Michal et al. "suggests" such a combination is Claim 20 of Michal et al., which claims: "The coated device of claim 1 wherein the therapeutic or diagnostic agent comprises one or more nitrogen oxide donating compounds selected from the group consisting of 2-methyl-2-nitrosopropane, S-Nitroso-N-acetyl-D,L-penicillamine, 3-morpholoinosydoimine, sodium nitrate, s-nitrosoglutatione, sodium nitroprusside, and nitroglycerine."

Applicants respectfully state that such a claim that lists multiple compounds as a potential therapeutic agent does not , by itself, and without additional support, teach or suggest a ***combination*** of two NO donor compounds. The "comprising" clause of Claim 20 within the Michal et al. disclosure is insufficient to meet the obviousness standard that the prior art reference (or references when combined) must teach or suggest all of the claimed features.

Thus, Michal et al. simply fails to provide an ***enabling*** disclosure for the specific features of the claimed medical article, wherein said medical article is adapted, after placement at a delivery position on or within the body of a patient, for local delivery of said first nitric oxide donor compound and a nitric oxide product of said first nitric oxide donor compound and for local delivery of said second nitric oxide donor compound and a nitric oxide product of said second nitric oxide donor compound. This lack of teaching, guidance, or even suggestion for a combination of two nitric oxide donor compounds is not surprising

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since the focus of Michal et al. is not at all about the delivery of nitric oxide. Rather, Michal et al. teaches a "hydrophilic coating which strongly adheres to a surface of a medical device...but [is] potentially releasably, adhered to the surface of a medical device." (Michal et al., col. 1, line 66 to col. 2, line 3).

The secondary reference, Sogo et al. does not remedy this deficiency. It also, does ***not*** teach a combination of NO donor compounds. The Examiner states that one of ordinary skill in the art may be "motivated by the teaching of Sogo et al. that these two NO donor compounds produce more relaxation of vessel walls than commonly used NO donors with prolonged sustained relaxation and dilatation of human arteries, and their use might improve the outcome of coronary artery bypass." Assuming arguendo that this were indeed the case, Sogo et al. presents nitrosoglutathione and N-(S-nitroso-N-acetylpenicillamine) as ***alternatives***, rather than ***as a combination***. Nowhere does Sogo et al. teach or even suggest of using ***both NO donors in conjunction with one another***. This is evidenced by all of the examples and experimental results in Sogo et al., in which response curves for RIG200 (N-(S-nitroso-N-acetylpenicillamine) are ***separate and distinct*** from response curves for GSNO (nitrosoglutathione) and there are no data or textual support for a combination of two or more NO donor compounds. (*See* Figures 3, 4, 5, 6, and their accompanying text).

The Examiner further argues that "the combination of the references teaches the same first nitric oxide donor and second nitric oxide donor as instantly claimed, therefore, the half-life, activity, release rates, and susceptibility to metal ion catalyst release are expected to be the same as those recited by the instant claims." Regarding this conclusion, it is respectfully submitted that the Examiner appears to be relying on inherency to remedy the deficiency of the combined references in teaching a combination of NO donor compounds. However, that which is inherent in the prior art, if not known at the same of the invention, cannot form a proper basis for rejecting the claimed invention as obvious under 35 U.S.C. §103. *See In re Shetty*, 566 F.2d 81, 86, 195 U.S.P.Q. 753, 756-57 (C.C.P.A. 1977).

A holding of inherency must flow as a necessary conclusion from the prior art, not simply a possible one. In re Rijckaert, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993), In re Oelrich, 666 F.2d 578, 581, 212 U.S.P.Q. 223 (Fed. Cir. 1981).

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In this regard, the Examiner's attention is directed to MPEP § 2112(IV):

> The fact that a certain result or characteristic ***may*** occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. To establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. . . .
>
> In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic ***necessarily*** flows from the teachings of the applied prior art.

(citations omitted)(emphasis added).

Since there is neither an express disclosure of the elements of Applicants' claimed invention nor a reasonable basis for a conclusion of inherency, reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 103(a) is respectfully requested.

Also, the addition of the disclosure of Sogo et al. to that of Michal et al. on its face relies upon the use of undue hindsight, which is prohibited. *See* Akso N.V. v. U.S. International Trade Commission, 808 F.2d 1241, 1480-81, 1 U.S.P.Q.2d, 1241, 1246 (Fed. Cir. 1986), *cert. denied,* 482 U.S. 909 (1987), Loctite Corp. v. Ultraseal Ltd., 781 F.2d 861, 874, 228 U.S.P.Q. 90-99 (Fed. Cir. 1985). Also see MPEP § 2142, second paragraph. Finally, the teachings of the references are not properly combinable without motivation and suggestion to combine them found in the references themselves. In re Jones, 958 F.2d 347, 351, 21 U. U.S.P.Q.2d 1941, 1943-44 (Fed. Cir. 1992), In re Fine, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596, 1598-99 (Fed. Cir. 1988).

In light of the above remarks, reconsideration and withdrawal of this rejection of the claims under 35 U.S.C. § 103 is respectfully requested.

For at least these reasons, Applicant respectfully submits that the claims are patentable over the cited references. Given the above remarks and the Terminal Disclaimer submitted herein, Applicant states that the Examiner's rejection under 35 U.S.C § 103(a) and

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the non-statutory double patenting rejection have been obviated and Applicant respectfully requests that the Examiner withdraw the rejections.

CONCLUSION

Applicants respectfully submit that all pending claims are in condition for allowance, early notification of which is earnestly solicited. Should the Examiner be of the view that an interview would expedite the application at large, request is made that the Examiner telephone the undersigned attorney at (908) 518-7700, ext. 7 in order to resolve any outstanding issues.

FEES

The Office is authorized to charge any fees required to deposit account number 50-1047.

Respectfully submitted,

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